



Design and synthesis of new octadentate macrocyclic chelators for ^{89}Zr

Bonnaud, Mylène; Fleurat-Lessard, Paul ; Severin, Gregory W.; Jensen, Andreas Tue Ingemann; Boschetti, Frédéric ; Denat , Franck

Published in:
Proceedings of European Molecular Imaging Meeting (EMIM) 2015

Publication date:
2015

[Link back to DTU Orbit](#)

Citation (APA):
Bonnaud, M., Fleurat-Lessard, P., Severin, G. W., Jensen, A. T. I., Boschetti, F., & Denat, F. (2015). Design and synthesis of new octadentate macrocyclic chelators for ^{89}Zr . In *Proceedings of European Molecular Imaging Meeting (EMIM) 2015*

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Design and synthesis of new octadentate macrocyclic chelators for ^{89}Zr

My  ne Bonnaud¹, Paul Fleurat-Lessard¹, Gregory W. Severin², Andreas I. Jensen², Fr  d  ric Boschetti³, Fran  ck Denat¹

¹ICMUB, 9 avenue Alain Savary, 21000 Dijon, France

²DTU NUTECH Technical University of Denmark, Frederiksborgvej 399, 4000 Roskilde, Denmark

³Chematech, 9 avenue Alain Savary, 21000 Dijon, France

Introduction

^{89}Zr is one of the most interesting radiometals for Positron Emission Tomography. This radionuclide possesses a low energy β positron which affords high resolution images, and a half life of 78.41 h, allowing a collection of images several days after injection, making this isotope particularly suitable for labelling biomolecules with long biodistribution time such as antibodies [1]. The most commonly used chelator for ^{89}Zr is Desferrioxamine (DFO) but one drawback of this latter is the partial decoordination of the metal in vivo. The challenge is to encapsulate ^{89}Zr to avoid release in organs while keeping good properties for molecular imaging.

Methods

Our concept uses macrocyclic polyamines as platforms to attach two kinds of coordinating moieties, i.e. picolinic acid and hydroxyquinoline. Four macrocycles were used: cyclen, cyclam, TACN and 13(ane)N4. The cycles were functionalized by addition of a p-nitrobenzyl group to allow further bioconjugation. Radiolabelling of some chelators with ^{89}Zr and competition experiments with DTPA were performed.

Results

8 new chelators were synthesized and metallated with $\text{Zr}(\text{acac})_4$. The macrocycles and the corresponding complexes were characterized by ESI, UV and NMR spectroscopies. Radiolabelling of 3 chelators with ^{89}Zr confirmed their promising coordinating properties. Competition with DTPA showed no transchelation for several days especially with the cyclam derivatives. DFT calculation had shown that the chelators are adapted to the complexation of Zr.

Conclusions

New macrocyclic chelators containing both pendant coordinating arms and a function for bioconjugation were prepared and characterized. The synthesis can be easily scaled-up. The first results showed that these chelators could be an alternative to DFO.

References

[1] Price E. W., Orvig C., *Chem. Soc. Rev.*, (43), 260-290 (2014)

Acknowledgement

Support was provided by Chematech Mdt, the University of Burgundy, CNRS and the Conseil R  gional de Bourgogne through the 3MIM project.

Keywords: ^{89}Zr , Macrocyclic chelator, PET tracer